# Organocatalytic Enantioselective [1,2]-Stevens Rearrangement of Azetidinium Salts

Ana De Oliveira Silva,[a]† Shruti A. Masand,[a]† Abdikani Omar Farah,[b] Jacqueline Laddusaw,[b] Kelvin Urbina,[a] Melanie Rodríguez-Alvarado,[a] Roger A. Lalancette,[a] Paul Ha-Yeon Cheong,*[b] and Stacey E. Brenner-Moyer*[a]

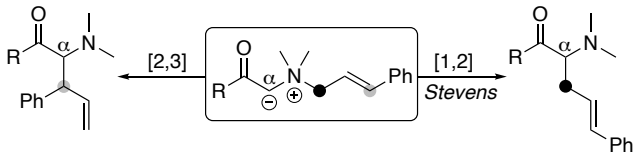
[a] Ana De Oliveira Silva, Shruti A. Masand, Kelvin Urbina, Melanie Rodríguez-Alvarado, Prof. Dr. Roger A. Lalancette, Prof. Dr. Stacey E. Brenner-Moyer
Department of Chemistry
Rutgers University
73 Warren Street, Newark, New Jersey, 07102, United States
E-mail: seb244@newark.rutgers.edu

[b] Jacqueline Laddusaw, Abdikani Omar Farah, Prof. Paul Ha-Yeon Cheong
Department of Chemistry
Oregon State University
153 Gilbert Hall, Corvallis, Oregon, 97331, United States
E-mail: cheongh@oregonstate.edu

Supporting information for this article is given via a link at the end of the document.

**Abstract:** An organocatalyzed enantioselective [1,2]-Stevens rearrangement of ammonium ylides is reported. Using an isothiourea Lewis base organocatalyst, azetidinium salts underwent ring expansion to generate 4-alkylideneproline derivatives in high yield and good er. Products are readily recrystallizable to provide er's of up to >99.5:0.5. Product configuration was established through X-ray crystallography and was opposite that predicted based on existing stereochemical models for this catalyst class. DFT calculations revealed that the facial selectivity of new bond formation is dictated by the pyramidalization of the enolate α-carbon in the ring-opening transition state. Notably, it is the catalyst benzylic hydrogen, and not the stereodirecting catalyst Ph, that influences this facial selectivity by stabilizing the developing pyramidalization of the enolate α-carbon in the transition state leading to the major enantiomer of product. Finally, under these reaction conditions, a tetrahydroisoquinolinium salt also underwent ring expansion to generate a benzazepine product as a single diastereomer in modest er. This result illustrates that this catalytic strategy for enantioselective [1,2]-Stevens rearrangement can be adapted for use with other synthetically- and medicinally-useful heterocyclic amine scaffolds.

The [1,2]-Stevens rearrangement (Scheme 1) of cyclic ammonium ylides leads to ring-expanded heterocyclic products.[1-2] As such, the applications of this transformation in alkaloid synthesis should be more widespread,[3] but instead have been limited by the near total void of catalytic asymmetric methods.[4] Thus, alkaloid syntheses employing this rearrangement either culminate in racemic natural products,[5] or necessitate enantiopure quaternary ammonium salt substrates to access natural products as single enantiomers.[6] The development of a catalytic asymmetric [1,2]-Stevens rearrangement of ammonium ylides has been hampered primarily by two considerations. First, a generally accepted mechanism for this transformation long remained elusive, with proposed models continuing to be discussed and debated in the literature as recently as 2020.[7] Further, a competing [2,3]-sigmatropic rearrangement is possible (Scheme 1), and is proposed to proceed via the same transition state, which complicates differentiation between these two reaction pathways.[8] As a consequence, the first catalytic asymmetric [2,3]-sigmatropic rearrangement of ammonium ylides was reported only within the past decade, and utilized an isothiourea organocatalyst.[9]




**Scheme 1.** Competing [1,2]-Stevens rearrangement and [2,3]-sigmatropic rearrangements of allylic ammonium ylides.

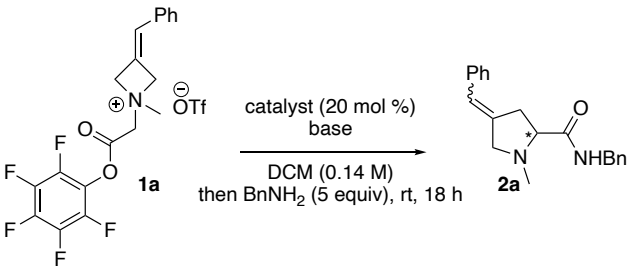
The first catalytic enantioselective [1,2]-Stevens rearrangement of ammonium ylides was reported very recently.[4] The corresponding rearrangement of oxonium- and sulfonium ylides have been known for longer, however, with the former first reported over half a century ago.[10-11] Notably, all of the catalytic enantioselective [1,2]-Stevens rearrangements of these -onium ylides proceed via chiral metal-bound or -associated -onium ylides. Typically, the reactive ylide is generated from insertion of a chiral metal catalyst into a diazo substrate and subsequent inter- or intramolecular trapping by a heteroatom,[4b-c,10a-d,11] with a couple recent examples intercepting this reactive species during a metal-catalyzed cascade reaction.[4a,10d] Since Lewis base organocatalysis had proven effective for enantioselective [2,3]-sigmatropic rearrangements of allylic ammonium ylides,[9] and

since this rearrangement shares a transition state with the [1,2]-Stevens rearrangement,[8] we wondered whether this class of organocatalysts might also be amenable to the latter transformation. Herein, we report a rare example of a catalytic enantioselective [1,2]-Stevens rearrangement of ammonium ylides, which employs a mechanistically distinct strategy from all previously reported [1,2]-Stevens rearrangements, namely, Lewis base organocatalysis.[4d]

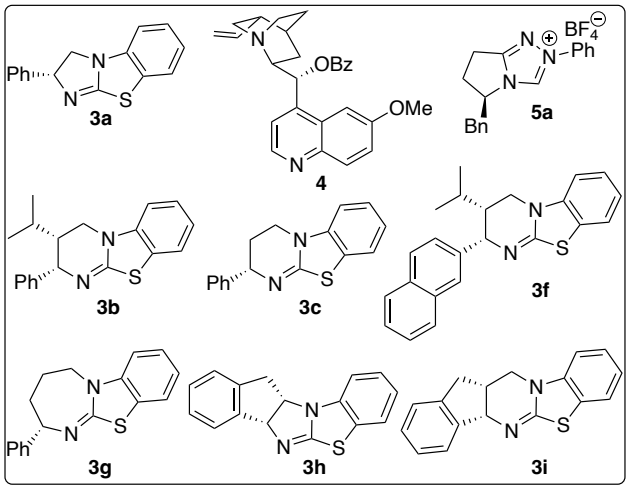
Azetidinium **1a** was envisioned as an appealing substrate for the development of the proposed transformation, as it is primed for ring expansion, and its geometric constraints should suppress a concerted [2,3]-sigmatropic rearrangement. Use of a triflate counterion was adopted after the observation of in-situ ring-opening of a related substrate by a more nucleophilic counterion, $Br^-$.[12] Several classes of Lewis base organocatalysts were examined using **1a** and related substrates.[12] Benzotetramisole catalyst **3a**, the optimal catalyst for the enantioselective [2,3]-sigmatropic rearrangements of allylic ammonium ylides,[9] rapidly generated product in high yield, but without enantioselectivity (entry 1, Table 1). A cinchona alkaloid catalyst, **4**, also provided racemic product (entry 2). Chiral NHC catalysts, including **5a**, afforded some degree of enantiocontrol in this transformation, but catalyst turnover (i.e., product yields higher than catalyst loadings) could not be achieved.[12] Even a full equivalent of **5a** generated **2a** in only 10% yield, but in excellent er (entry 3). Remarkably, while benzotetramisole catalyst **3a** provided racemic product, the corresponding ring-expanded catalysts, including **3b**, produced **2a** in moderate er (entry 4). Lowering the reaction temperature to -30 ºC led to product formation in high yield and considerably improved er (entry 5). At -30 ºC, use of related catalyst **3c**, which lacks a vicinal stereocenter, had minimal impact on product yield or er (entry 6). Replacing the phenyl group with a napthyl group, as in catalyst **3f**, had no impact on er, but decreased product yields (entry 7). Further ring-expanded catalyst **3g**, reported here for the first time, resulted in racemic products (entry 8). The product er could be further significantly improved by lowering the equivalents of base, albeit at the expense of a reduced product yield (entry 9). Under these conditions an isothiourea catalyst (**3h**) recently introduced by Melchiorre and coworkers,[13] in addition to the corresponding ring-expanded catalyst (**3i**), were evaluated, but neither provided results superior to **3b** (entries 10-11). Interestingly, at reaction temperatures at or below -50 ºC, only one product diastereomer was formed, indicating a kinetic resolution may be possible (entry 12). Back at -30 ºC, a screen of a variety of bases revealed that use of DABCO led to improved product er, but only moderate yields (entry 13), which could not be improved through variation of base equivalents, or of the reaction time, temperature, or solvent.[12] Finally, increasing reaction time to 48 h increased the yield of product without compromising er, and the conditions in entry 14 were identified as the optimal reaction conditions for this transformation.

Substrates similar to **1a**, but with a variety of substituted phenyl groups were first evaluated. Substrates, **1**, in which R ≠ $R^1$ are stereoisomeric mixtures (Scheme 2). Consequently, products arising from these substrates are diastereomeric, and are generated as a 1:1 mixture of *E*:*Z* alkene isomers. In all cases except **2g** and **2m**, product diastereomers were readily separable via conventional silica gel column chromatography. Substrates containing unsubstituted phenyl groups and those with *para*-halo-

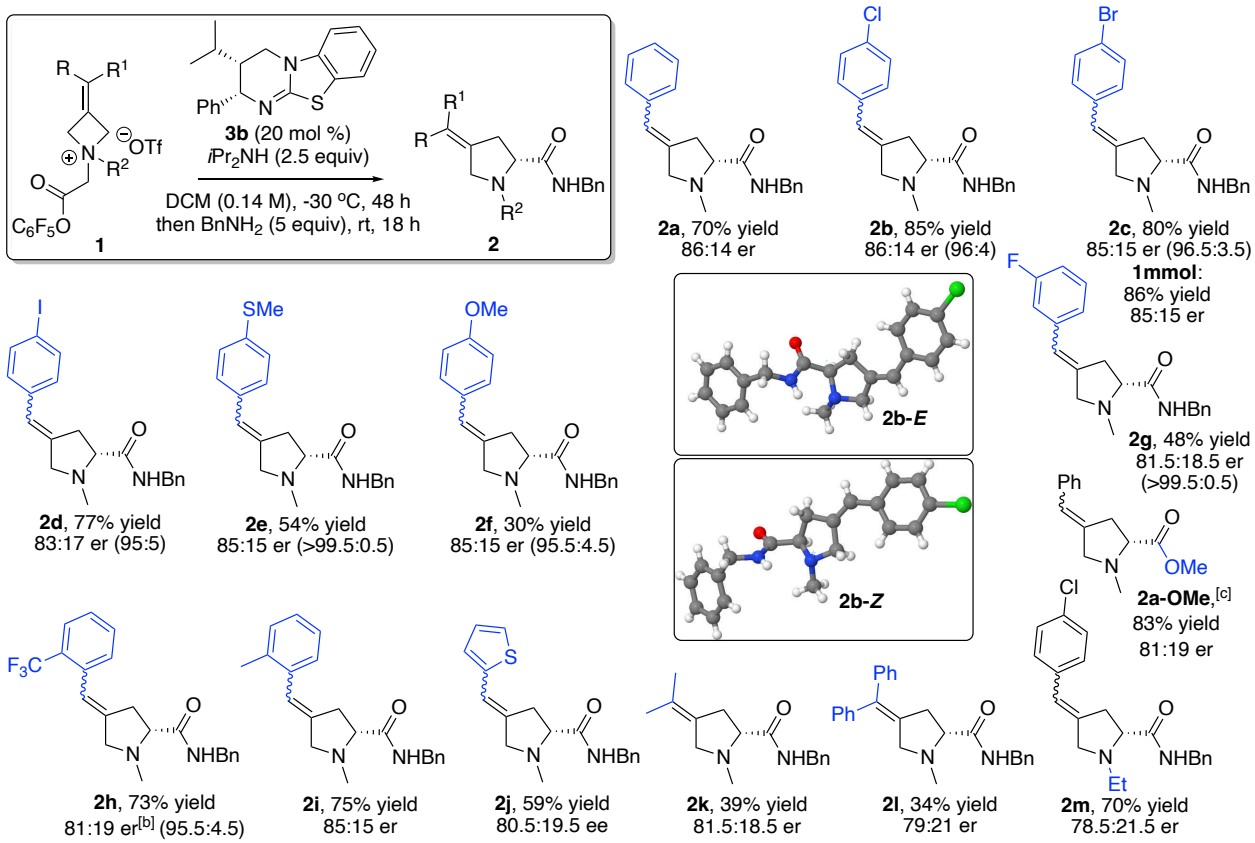
**Table 1.** Summary of key reaction optimizations.[a]




| entry | cat | base | base equiv | temp (ºC) | time | yield (%)[a] | er[b] |
|---|---|---|---|---|---|---|---|
| 1 | **3a** | *i*Pr$_2$NH | 5 | rt | 5 min | 78 | racemic |
| 2 | **4** | *i*Pr$_2$NH | 1.5 | rt | 30 min | nd | racemic |
| 3[c] | **5a** | *i*Pr$_2$NEt | 1.5 | 0 | 48 h | 10 | 95:5 |
| 4[d] | **3b** | *i*Pr$_2$NH | 5 | rt | 30 min | 88 | 70:30 |
| 5[d] | **3b** | *i*Pr$_2$NH | 5 | -30 | 24 h | 91 | 79.5:20.5 |
| 6[d] | **3c** | *i*Pr$_2$NH | 5 | -30 | 24 h | 87 | 77:23 |
| 7[d] | **3f** | *i*Pr$_2$NH | 5 | -30 | 24 h | 30 | 78:22 |
| 8[d] | **3g** | *i*Pr$_2$NH | 5 | -30 | 24 h | 20 | racemic |
| 9[d] | **3b** | *i*Pr$_2$NH | 2.5 | -30 | 24 h | 65 | 86:14 |
| 10[d] | **3h** | *i*Pr$_2$NH | 2.5 | -30 | 24 h | 68 | 84.5:15.5 |
| 11[d] | **3i** | *i*Pr$_2$NH | 2.5 | -30 | 24 h | 79 | 74:26 |
| 12[d-e] | **3b** | *i*Pr$_2$NH | 2.5 | -50 | 24 h | 30 | 86:14 |
| 13[d] | **3b** | DABCO | 2.5 | -30 | 48 h | 46 | 90:10 |
| 14[d] | **3b** | *i*Pr$_2$NH | 2.5 | -30 | 48 h | 70 | 86:14 |




[a] Yield=isolated yield. [b] er determined by chiral HPLC. [c] using **5a** (1 equiv), substrate **1ac** (*para*-nitrophenyl ester), and solvent=MeCN. [d] with 3Å mol sieves and distilled base. [e] Only one diastereomer formed.




**Scheme 2.** Azetidinium salt substrate scope.[a] [a] Yields are combined isolated yields of E/Z alkene isomers; er is for *E* diastereomer as determined by chiral HPLC; er for *Z* diastereomer, where quantified,[12] was identical; er in parentheses is after recrystallization. [b] Reaction run at -40 °C. [c] Quenched with MeOH instead of $BnNH_2$.

gen substituents underwent the [1,2]-Stevens rearrangement in high yield and er (**2a-d**). As evidenced by results using **2c**, the reaction can be readily scaled up. Substrates with phenyl groups with electron-donating *para*-substituents also formed pyrrolidine products (**2e-f**) in high er, but in reduced yield. Electron-withdrawing substituents at the *meta*- or *ortho*-positions resulted in a reduced er of products (**2g-2h**). The corresponding product arising from a *p*-$NO_2$ substrate (**1n**)[12] was generated in low yield and was prone to decomposition (not shown). Pleasingly, *ortho*-substitution did not hamper product (**2i**) formation or enantioselectivity, presumably since this position is far removed from the reactive centers. A heteroaromatic substrate was compatible with these reaction conditions, as were disubstituted olefins, however ring-expanded products (**2j-2l**) were generated in lower er and, in the latter cases, reduced yield. Not surprisingly, altering the group on the azetidinium N, being one of the reactive centers, had a pronounced impact on product er (**2m**). An alternate quench with MeOH, instead of $BnNH_2$, provided direct access to the corresponding ester product, **2a-OMe**.

Since most of the products were solids, the er could be substantially improved after a single recrystallization. As representative examples, the er after a single recrystallization appears in parentheses for select products in Scheme 2. Moreover, the ease of separating diastereomers via column chromatography and of crystalline product formation facilitated the assignment of configuration in products. X-ray crystallography of the *E* and *Z* diastereomers of **2b** established the alkene geometry and confirmed that the chiral center in both diastereomers had the same configuration (i.e., *R*).[14] The alkene geometry and chiral center in all other products were assumed to be analogous.

Curiously, the *R* configuration of products was opposite that predicted by existing models for stereoinduction by catalyst **3b**. To investigate the origins of the observed stereoselectivity in this benzotetramisole (**LB**) catalyzed [1,2]-Stevens rearrangement, Density Functional Theory (DFT) was used. Specifically, we used the PBE level of theory with Grimme's empirical dispersion forces with Becke Johnson dampening parameter (D3BJ) and the 6-31G(d) basis set. All computations were performed under SMD solvation with dichloromethane solvent at 243.15 K.[15-18]

Azetidinium **1k,** which features a symmetric alkene on the azetidine, was selected for computational study. Additionally, the system was investigated both with and without the triflate counterion.

The catalytic cycle (Figure 1) begins with acylation of **LB** by **1k,** followed by deprotonation of the α-carbon to give the **ammoniom ylide**. Initial C–N bond cleavage of the azetidinium ring leads to the ring-opened **allyl-anion iminium** intermediate. Subsequent ring-closure and $C_6F_5O^-$ exchange releases the catalyst, and final product pyrrolidine **2k** is ultimately generated after the reaction quench with benzylamine.

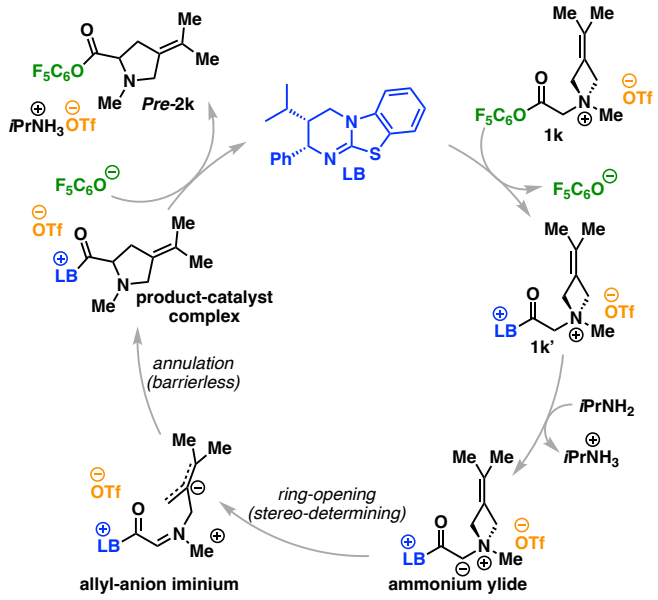



**Figure 1.** Catalytic cycle of the [1,2]-Stevens rearrangement catalyzed by benzotetramisole (LB).

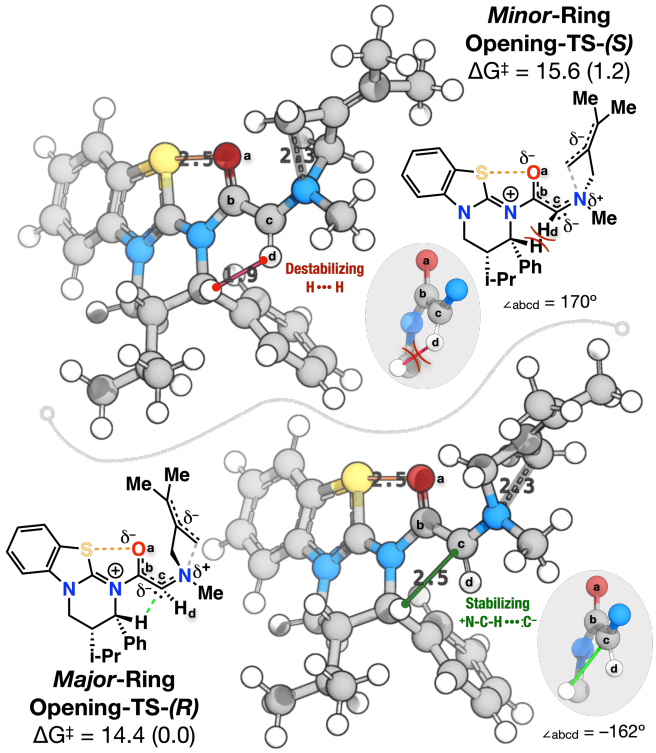



**Figure 2.** Computed major and minor transition structures for the C-N bond cleavage step.

The investigation focused on the ring-opening and -closing steps as those determine the stereochemical outcome of the reaction. Interestingly, the annulation process was found to be barrierless, likely due to the ionic nature of the transient **allyl-anion iminium**. This strongly suggests that the C–N bond cleavage and the subsequent annulation steps occur on the same face of the enolate.

To gain insight into the origins of stereoselectivity, we therefore examined the major and minor DFT transition structures for the ring-opening (Figure 2). The **Major-TS-*(R)*** leads to the major product ***Pre*-2k-*(R)*** and had a barrier of 14.4 kcal/mol. In comparison, **Minor-TS-*(S)***, which leads to the minor product ***Pre*-2k-*(S)*** had a barrier of 15.6 kcal/mol ($\Delta\Delta G^{‡}$ = 1.2 kcal/mol, 92.5:7.5 er)**.** The DFT selectivity is in reasonable agreement with the experimental observations of 81.5:18.5 er (i.e. $\Delta\Delta G^{‡}$ = 0.72 kcal/mol).

The major and minor transition structures are nearly identical, except for the environment around the benzylic hydrogen of the catalyst. In the **Major-TS-*(R)***, the enolate α-carbon is in close proximity to the benzylic hydrogen of the catalyst (2.5 Å). In contrast, in the **Minor-TS-*(S)***, it is the hydrogen on the enolate α-carbon that is in closer proximity with the catalyst benzylic hydrogen (1.9 Å). Upon closer examination, in the **Major-TS-*(R)***, the enolate α-carbon is pyramidalized such that the putative lone pair is directed towards the catalyst benzylic hydrogen – a stabilizing interaction. In contrast, in the **Minor-TS-*(S)***, the pyramidalization is opposite, forcing the hydrogen on the enolate α-carbon towards the catalyst benzylic hydrogen – a destabilizing interaction.

The ChelpG charges of the ammonium ylide were then computed. The α-carbon was found to have a substantial negative charge of –0.65, consistent with an enolate carbanion (See Supporting Information).[19] Both the hydrogen on the enolate α-carbon and the catalyst benzylic hydrogen exhibit positive charge character (0.09 and 0.16, respectively). This reinforces the above supposition that in the **Major-TS-*(R)***, the lone-pair is stabilized by electrostatic interaction with the benzylic hydrogen of the catalyst ($^{+}$N-C-H ••• :C$^{-}$, 2.5 Å). Further, this interaction is absent in the **Minor-TS-*(S)***, and in its place, a destabilizing hydrogen-hydrogen interaction is instead found (H ••• H, 1.9 Å).

Thus, stereocontrol in this system is governed by the direction of pyramidalization of the enolate α-carbon in the ring-opening transition state. This sterocontrolling pyramidalization phenomenon was first observed by Houk and coworkers, in model alkene and alkyne systems (Figure 3a).[20] Nucleophilic addition to π-systems caused a lone-pair to develop *anti* to the incoming nucleophile, pyramidalizing the forming carbanion. In our system (Figure 3b), an iminium is forming as the C–N bond breaks. Once again, the lone pair is *anti* to this breaking bond, thereby pyramidalizing the enolate α-carbon. In the context of the chiral isothiourea catalyst (Figure 3c), cleavage of the C-N bond *anti* to the stereodirecting phenyl group of the isothiourea catalyst forces pyramidalization to occur in such a way that creates a destabilizing hydrogen-hydrogen interaction (H ••• H, 1.9 Å). However, if the cleavage of the C-N bond occurs *syn* to the stereodirecting catalyst phenyl, the pyramidalization puts the enolate α-carbon anion in close proximity to the catalyst benzyl hydrogen, a stabilizing electrostatic interaction ($^{+}$N-C-H ••• :C$^{-}$, 2.5 Å). Cleavage of the C-N bond *syn* to the stereodirecting catalyst phenyl culminates in subsequent barrierless C-C bond formation (annulation) *syn* to the stereodirecting catalyst phenyl, which is counter to what is ordinarily observed with this catalyst class.

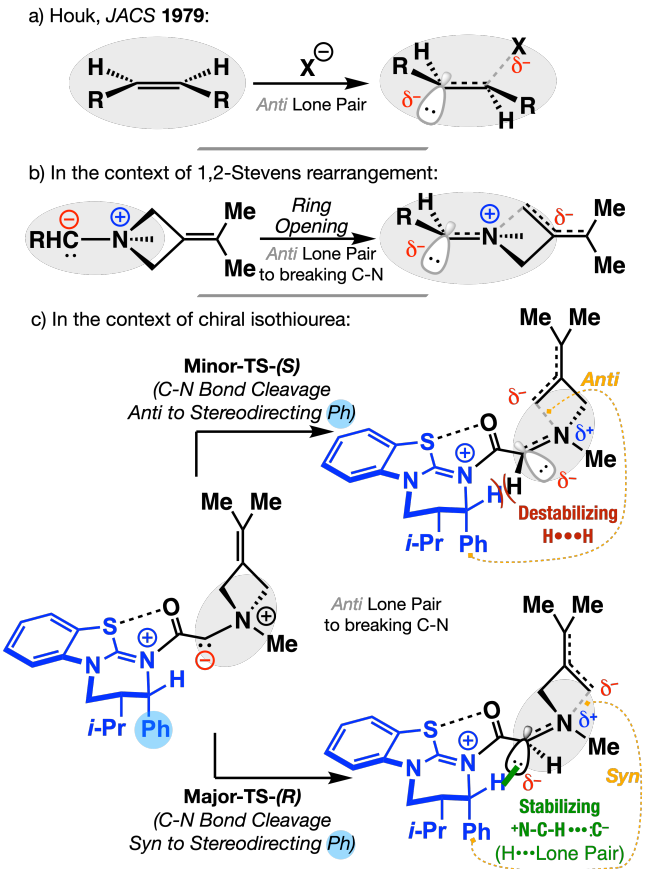
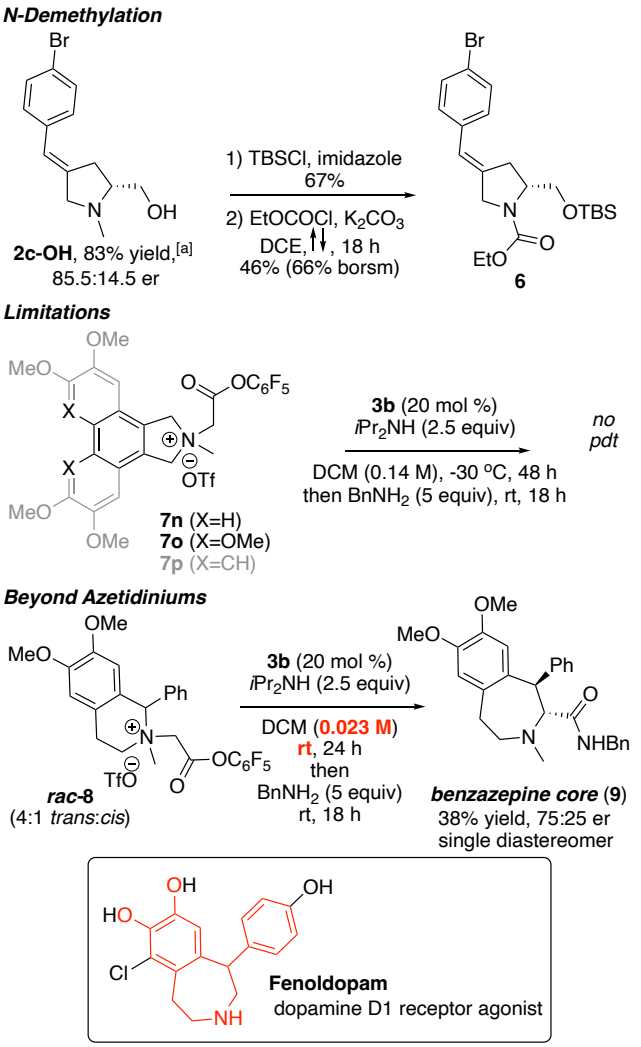



**Figure 3.** Geometries of complexes between nucleophiles and alkenes (a), azetidinium (b), and azetidinium with the chiral isothiourea (c).

Finally, to explore the potential synthetic utility of the reaction conditions developed for this Lewis base-catalyzed [1,2]-Stevens rearrangement, we considered both elaboration of pyrrolidine products as well as non-azetidinium salt substrates. As mentioned earlier, direct access to carboxylic acid derivatives beyond amides, such as ester **2a-OMe**, can be acheived by judicious choice of nucleophilic quench. Additionally, a reductive quench of the reaction provided the corresponding alcohol, **2c-OH** (Scheme 3), in identical yield and er to that of the amide product. Importantly, following protection of the free alcohol in **2c-OH**, this product readily underwent *N*-demethylation to provide a more versatile carbamate-protected pyrrolidine, **6**. Next, when release of ring strain was eliminated as a driving force for rearrangement, as in isoindolinium salt **7n**, product formation did not occur under these reaction conditions, nor at higher temperatures. Highly electron-rich isoindolinium **7o**[21] similarly failed to undergo ring expansion, as did **7p**,[5d] despite enhanced stabilization of the benzylic reactive center in the latter, by virtue of reduced aromatic stabilization of the central ring in the phenanthrene system. However, rearrangement of larger ring systems was facilitated by the addition of a second activating group on the reactive center, as in ***rac*-8**.[22] Promisingly, even under conditions unoptimized for this substrate class, tetrahydroisoquinolinium substrate ***rac*-8** afforded a single diastereomer of product in modest er. The reaction was run at rt and under dilute conditions, to promote the intramolecular reaction, which is no longer exclusively favored in the absence of ring strain. Product **9** contains a bicyclic core common in benzazepine drugs, such as Fenoldopam, a D1 receptor agonist. This result demonstrates that, with suitable reoptimization, this organocatalytic enantioselective [1,2]-Stevens rearrangement will be amenable to other synthetically- and medicinally-relevant amine scaffolds.




**Scheme 3.** Product elaboration and evaluation of non-azetidinium salt substrates. [a] Combined isolated yield of E/Z alkene isomers after quenching reaction at -30 °C by addition of pre-cooled THF and $LiAlH_4$.

In conclusion, we have developed an organocatalyzed enantioselective [1,2]-Stevens rearrangement of azetidinium salts. Reaction products are 4-alkylideneproline amides, which are generated in up to 86% yield and in up to 86:14 er, with recrystallization enhancing er up to >99.5:0.5. The corresponding ester and alcohol products can be accessed directly from the catalytic reaction by modifying the nucleophilic quench. Interestingly, DFT calculations showed the major ***R*** product configuration arose from a stabilizing lone-pair•••H interaction in the major ring-opening transition state, which is absent in the transition state (destabilizing H•••H) that leads to the minor ***S*** product. Remarkably, the two most influential enantiodetermining factors are the pyramidalization of the enolate α-carbon in this ring-opening transition state and the catalyst benzylic hydrogen,

not the stereodirecting catalyst Ph. Further, product derivatives underwent *N*-demethylation to provide the corresponding *N*-carbamate product, affording an orthogonally protected 4-alkylideneprolinol amenable to further synthetic elaboration. Finally, ring expansion of a tetrahydroisoquinolinium salt under these reaction conditions highlights the potential of this catalytic strategy to be extended to other cyclic amine scaffolds.

## Acknowledgements

This research was supported by the National Science Foundation (S.E.B.-M., CHE-1955044). PHYC is the Bert and Emelyn Christensen professor of OSU, and gratefully acknowledges financial support from the Vicki & Patrick F. Stone family and the National Science Foundation (NSF, CHE-1352663). AOF also acknowledges financial support from The Larry W. Martin & Joyce B. O'Neill Endowed Fellowship.

† Denotes equal contribution.

**Keywords:** Asymmetric Catalysis • Nitrogen Heterocycles • Organocatalysis • Rearrangement • Ring Expansion

[1] T. S. Stevens, E. M. Creighton, A. B. Gordon, M. MacNicol, *J. Chem. Soc.* **1928**, 3193-3197.

[2] For recent reviews, see: a) C. Empel, S. Jana, R. M. Koenigs, *Synthesis* **2021**, *53*, 4567-4587; b) C.-Y. Shi, B. Zhou, M.-Y. Teng, L.-W. Ye, L.-W. *Synthesis* **2023**, *55*, 2118-2127.

[3] For reviews, see: a) J. A. Vanecko, H. Wan, F. G. West, *Tetrahedron* **2006**, *62*, 1043-1062; b) Z. Schwartz, C. Valiton, M. Lovasz, A. G. Roberts, A. G. *Synthesis* **2023**, *55*, DOI: 10.1055/s-0042-1751446.

[4] a) K. Hong, S. Zhou, W. Hu, X. Xu, *Org. Chem. Front.* **2020**, *7*, 1327-1333; b) D. C. Miller, R. G. Lal, L. A. Marchetti, F. H. Arnold, *J. Am. Chem. Soc.* **2022**, *144*, 4739-4745; c) K. Wang, L. Yang, Y. Li, H. Li, Z. Liu, L. Ning, X. Liu, X. Feng, X. *Angew. Chem. Int. Ed.* **2023**, e202307249; d) Through personal correspondance with Andrew D. Smith (University of St Andrews) during the preparation of this manuscript, we are aware of his forthcoming submission describing a related strategy for transformation of a different system(s); we will cite him accordingly here when e.g., DOI information becomes available.

[5] See, for example: a) J.-P. Liou, C.-Y. Cheng, *Tetrahedron Lett.* **2000**, *41*, 915-918; b) J. A. Vanecko, F. G. West, *Org. Lett.* **2005**, *7*, 2949-2952; c) M. Valpuesta, M. Ariza, A. Diaz, G. Torres, R. Suau, *Eur. J. Org. Chem.* **2010**, 638-645; d) G. Lahm, A. Stoye, T. Opatz, *J. Org. Chem.* **2012**, *77*, 6620-6623; e) J. C. Orejarena Pacheco, G. Lahm, T. Opatz, *J. Org. Chem.* **2013**, *78*, 4985-4992; f) Q.-X. Lin, T.-L. Ho, *Tetrahedron* **2013**, *69*, 2996-3001.

[6] See, for example: a) F. G. West, B. N. Naidu, *J. Am. Chem. Soc.* **1994**, *116*, 8420-8421; b) S. Hanessian, M. Mauduit, *Angew. Chem. Int. Ed.* **2001**, *40*, 3810-3813; c) Y. Zhang, Y. Xue, G. Li, H. Yuan, T. Luo, *Chem. Sci.* **2016**, *7*, 5530-5536.

[7] See, for example: a) S. N. Hosseini, J. R. Johnston, F. G. West, *Chem. Commun.* **2017**, *53*, 12654-12656; b) S. Bhakat, *J. Chem. Pharm. Res.* **2011**, *3*, 115-121, and references cited therein; c) D. Baidilov, *Synthesis* **2020**, *52*, 21-26, and references cited therein.

[8] a) B. Biswas, S. C. Collins, D. A. Singleton, *J. Am. Chem. Soc.* **2014**, *136*, 3740-3743; b) B. Biswas, D. A. Singleton, *J. Am. Chem. Soc.* **2015**, *137*, 14244-14247.

[9] a) T. H. West, D. S. B. Daniels, A. M. Z. Slawin, A. D. Smith, *J. Am. Chem. Soc.* **2014**, *136*, 4476-4479; b) T. H. West, D. M. Walden, J. E. Taylor, A. C. Brueckner, R. C. Johnston, P. H.-Y. Cheong, G. C. Lloyd-Jones, A. D. Smith, *J. Am. Chem. Soc.* **2017**, *139*, 12, 4366-4375.

[10] Catalytic enantioselective [1,2]-Stevens rearrangement of oxonium ylides: a) H. Nozaki, H. Takaya, S. Moriuti, R. Noyori, *Tetrahedron* **1968**, *24*, 3655-3669; b) K. Ito, T. Katsuki, *Chem. Lett.* **1994**, 1857-1860; c) M. P. Doyle, D. G. Ene, D. C. Forbes, J. S. Tedrow, *Tetrahedron Lett.* **1997**, *38*, 4367-4370; d) M. M.-C. Lo, G. C. Fu, *Tetrahedron* **2001**, *57*, 2621-2634; e) F.-L. Hong, C.-Y. Shi, P. Hong, T.-Y. Zhai, X.-Q. Zhu, X. Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2022**, *61*, e202115554.

[11] Catalytic enantioselective [1,2]-Stevens rearrangement of sulfonium ylides: a) J.-P. Qu, Z.-H. Xu, J. Zhou, C.-L. Cao, X.-L. Sun, L.-X. Dai, Y. Tang, *Adv. Synth. Catal.* **2009**, *351*, 308-312; b) H. Yuan, T. Nuligonda, H. Gao, C.-H. Tung, Z. Xu, *Org. Chem. Front.* **2018**, *5*, 1371-1374; c) L. Hu, J. Li, Y. Zhang, X. Feng, X. Liu, *Chem. Sci.* **2022**, *13*, 4103-4108.

[12] See Supporting Information for full details.

[13] W. C. Hartley, F. Schiel, E. Ermini, P. Melchiorre, *Angew. Chem. Int. Ed.* **2022**, *61*, e202204735.

[14] Deposition numbers 2300729 (for **2b-*Z***) and 2300730 (for **2b-*E***) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

[15] J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* **1996**, *77*, 3865-3868.

[16] S. Grimme, S. Ehrlich, L. Goerigk, *J. Comput. Chem.* **2011**, *32*, 1456-1465.

[17] G. A. Petersson, A. Bennett, T. G. Tensfeldt, M. A. Al-Laham, W. A. Shirley, J. A. Mantzaris, *J. Chem. Phys.* **1988**, *89*, 2193-2218.

[18] G. A. Petersson, M. A. Al-Laham, *J. Chem. Phys.* **1991**, *94*, 6081-6090.

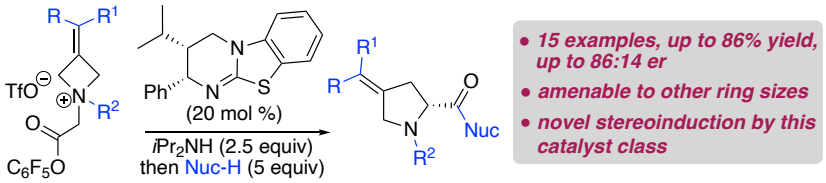
[19] C. M. Breneman, K. B. Wiberg, *J. Comput. Chem.* **1990**, *11*, 361-373.

[20] R. W. Strozier, P. Caramella, K. N. Houk, *J. Am. Chem. Soc.* **1979**, *101*, 1340–1343.

[21] E. Tayama, K. Takedachi, H. Iwamoto, E. Hasegawa, *Tetrahedron Lett.* **2012**, *53*, 1373-1375.

[22] M. Valpuesta, M. Ariza, A. Díaz, R. Suau, *Eur. J. Org. Chem.* **2010**, 4393-4401.

## Entry for the Table of Contents




- *15 examples, up to 86% yield, up to 86:14 er*
- *amenable to other ring sizes*
- *novel stereoinduction by this catalyst class*

**Even Stevens**: An organocatalyzed enantioselective [1,2]-Stevens rearrangement of ammonium ylides is reported. A tetrahydroisoquinolinium salt also underwent ring expansion, generating a benzazepine product and highlighting the potential to adapt this catalytic strategy for rearrangement of other useful heterocyclic amine scaffolds. Computational models for the observed product configuration, which was opposite that expected, also appear herein.

Institute and/or researcher Twitter usernames: ((optional))